Articles

Dietary fibre and colorectal adenoma in a colorectal cancer early detection programme

Ulrike Peters, Rashmi Sinha, Nilanjan Chatterjee, Amy F Subar, Regina G Ziegler, Martin Kulldorff, Robert Bresalier, Joel L Weissfeld, Andrew Flood, Arthur Schatzkin, Richard B Hayes, for the Prostate, Lung, Colorectal, and Ovarian Cancer Screening Trial Project Team

Summary

Background Although dietary fibre has been reported to have no association with colorectal adenoma and cancer, in some studies this topic remains controversial.

Methods We used a 137-item food frequency questionnaire to assess the relation of fibre intake and frequency of colorectal adenoma. The study was done within the Prostate, Lung, Colorectal, and Ovarian (PLCO) Cancer Screening Trial, a randomised controlled trial designed to investigate methods for early detection of cancer. In our analysis, we compared fibre intake of 33 971 participants who were sigmoidoscopy-negative for polyps, with 3591 cases with at least one histologically verified adenoma in the distal large bowel (ie, descending colon, sigmoid colon, or rectum). Odds ratios were estimated by logistic regression analysis.

Findings High intakes of dietary fibre were associated with a lower risk of colorectal adenoma, after adjustment for potential dietary and non-dietary risk factors. Participants in the highest quintile of dietary fibre intake had a 27% (95% CI 14–38, p_{trend}=0·002) lower risk of adenoma than those in the lowest quintile. The inverse association was strongest for fibre from grains and cereals and from fruits. Risks were similar for advanced and non-advanced adenoma. Risk of rectal adenoma was not significantly associated with fibre intake.

Interpretation Dietary fibre, particularly from grains, cereals, and fruits, was associated with decreased risk of distal colon adenoma.

Lancet 2003; **361:** 1491–95
See Commentary page 1487

Divisions of Cancer Epidemiology and Genetics (U Peters PhD, R Sinha PhD, N Chatterjee PhD, R G Ziegler PhD, A Flood PhD, A Schatzkin MD, R B Hayes PhD); **and Cancer Control and Population Sciences** (A F Subar PhD), **National Cancer Institute, US National Institutes of Health, DHHS, MD, USA; University of Connecticut School of Medicine, Farmington, CT** (M Kulldorff PhD); **University of Texas, MD Anderson Cancer Center, Houston, TX** (Prof R Bresalier MD); **University of Pittsburgh, Pittsburgh, PA** (J L Weissfeld MD)

Correspondence to: Dr Ulrike Peters, Nutritional Epidemiology Branch, Division of Cancer Epidemiology and Genetics, National Cancer Institute, 6129 Executive Blvd, EPS 3024 Rockville, MD 20892-7273, USA
(e-mail: petersu@mail.nih.gov)

Introduction

More than 30 years ago, Burkitt[1] noted the association of high dietary fibre intake with a low incidence of large bowel cancer in Africa. Since then, the association between fibre and colorectal neoplasia has been intensively investigated. Several mechanisms for a beneficial effect of fibre have been proposed, including dilution and binding of potential carcinogens, decreased transit time, reduced production of secondary bile acids because of primary bile acid binding, and fermentation of fibre to short-chain fatty acids.[2]

As precursor lesions of colorectal cancer, adenomas are an informative endpoint for colon carcinogenesis. The results of several case-control studies[3–12] have shown inverse associations between fibre and colorectal adenoma. In a large cohort study, fibre,[13] particularly fruit fibre, was inversely associated with sigmoidoscopy-detected adenoma in men, whereas a cohort study[14] in women found no association for colorectal adenoma. Intervention studies have shown no protective association of either a high-fibre diet[15,16] or supplementary fibre[17,18] with adenoma recurrence, although the results of one study showed a non-significant risk reduction for recurrent large adenomas.[18] In one study[19] risk for adenoma recurrence was significantly increased in a group given ispaghula husk fibre, but only in participants with high calcium intake. Bingham and colleagues[20] have reviewed the investigations of fibre and colorectal cancer in this issue of *The Lancet*. Because of the continuing controversy about fibre and adenoma, we assessed the relation of fibre intake to risk of colorectal adenoma in a large clinical trial of more than 3500 cases of distal adenoma that had been detected through screening and in almost 34 000 sigmoidoscopy-negative controls.

Methods

Study population

This study was done in participants randomised to the screening group of the Prostate, Lung, Colorectal, and Ovarian (PLCO) Cancer Screening Trial,[21] a multisite investigation (Birmingham, AL; Denver, CO; Detroit, MI; Honolulu, HI; Marshfield, WI; Minneapolis, MN; Pittsburgh, PA; Salt Lake City, UT; St Louis, MO; and Washington, DC) of the effectiveness of early detection for these cancers. As part of the PLCO Trial, flexible sigmoidoscopic visualisation of the distal colon (60 cm) was done at study entry in participants in the screening group. Those with lesions suspect for colorectal neoplasia (ie, sigmoidoscopically visualised polypoid lesions or masses) were referred for endoscopic follow-up, including histopathological examination. The PLCO trial obtained all available medical and pathological reports on all lesions removed during the diagnostic endoscopy and related surgical procedures. This information was abstracted and coded by trained medical abstractors. As an adjunct to the trial, questionnaire data and biological samples were

For personal use. Only reproduce with permission from The Lancet Publishing Group.

obtained from participants, for substudies of the causes.[22] Study participants provided written informed consent, after approval by the institutional review boards of the US National Cancer Institute and the ten screening centres.

Between September, 1993, and September, 2000, 56 176 men and women aged 55–74 had successful sigmoidoscopic screening examinations (insertion to at least 50 cm with >90% of mucosa visible or a suspect lesion identified). Of these, 51 028 participants (91%) completed the baseline food frequency and other risk-factor questionnaires.

We excluded 7417 participants for the following reasons if they had missing data for food frequency for more than seven items in the food frequency questionnaire (n=451); extreme values for energy intake (lowest and highest 1% on sex-specific energy intake; n=947); previous history of cancer, except basal-cell skin cancer (n=2329); or self-reported history of ulcerative colitis, Crohn's disease, familial polyposis, colorectal polyps, or Gardner's syndrome (n=4616).

After these exclusions, 43 611 participants remained. We studied 3591 cases with pathologically verified distal (left-sided) adenomatous polyps of the descending colon, sigmoid colon, or rectum and 33 971 controls with no suspicion of neoplasia of the distal colon on either sigmoidoscopic screening exam (n=32 415) or follow-up endoscopy after positive screening (n=1556). Adenomas were defined as advanced (n=1395) if they were large (⩾1 cm), had high-grade dysplasia (including cancer-in-situ), or had villous elements (including tubulovillous adenomas). We excluded participants with distal hyperplastic polyps only (n=1501); with distal benign lesions not further specified (n=108), colorectal lesions (polyps or cancer) of unknown location (n=279); or distal polyps of uncertain histology or cancer (n=1513). We also excluded 83 participants with histology data pending at the time of analysis and 2565 participants who were under medical follow-up without additional endoscopy after a positive screening (on sigmoidoscopy screening, 1869 [73%] of these participants had a polyp that was smaller than 5 mm in largest dimension). The data for this analysis were last updated in September, 2002.

Procedures

At the initial screening, participants filled out a questionnaire on sociodemographic factors, current and past smoking behaviour, history of cancer and other diseases, use of selected drugs, and recent history of screening examinations. We assessed usual dietary intake over the 12 months before enrolment by a food-frequency questionnaire that included 137 individual food items, 77 of which queried about usual portion size (http://www3.cancer.gov/prevention/plco/DQX.pdf). The questionnaire was adapted from the Willet and Block food frequency questionnaires, which have been widely used in epidemiological studies in the USA.[7,8,14,16] The dietary questionnaire also contained ten questions about meat cooking practices and 14 questions about intake of vitamin and mineral supplements. We calculated nutrient and food group values on the basis of the method developed by Subar and colleagues,[23] using US dietary data and the pyramid food group servings database from US Department of Agriculture (CSFII),[24] which determines dietary fibre by enzymatic-gravimetric methods. We created specific fibre food groups on the basis of the pyramid food groups for grain and cereal fibre, vegetable fibre, legume fibre, and fruit fibre by calculating the fibre content of each food item assigned to a specific fibre food group and multiplying this value by the amount of the food item consumed. For mixed dishes, we used recipe data to apportion the fibre content to the specific fibre food groups.

Statistical analysis

We first used a non-parametric regression model (Kernel smoothing) to visually assess the linearity of the dose-response relation between grams of fibre intake per day and prevalence of adenoma. Using logistic regression analysis we calculated prevalence odds ratios for fibre intake, coded continuously or as quintiles. Base logistic models were calculated, adjusting for age at randomisation, sex, study centre, and total energy intake (kcal/day). Energy adjustment relied on the standard model; use of the residual and partition methods yielded similar results.

	Overall (n=33 971)	**Total fibre intake**	
		Lowest quintile (n=6793)	Highest quintile (n=6794)
Characteristics			
Controls	33 971	6793	6794
Age (years)	62·8 (5·3)	62·1 (5·3)	63·3 (5·3)
Women	16 536 (49%)	3971 (58%)	2363 (35%)
Ethnic origin			
American Indian or Alaskan native	70 (<1%)	21 (<1%)	19 (<1%)
Asian	1414 (4%)	364 (5%)	285 (4%)
Hispanic	497 (2%)	118 (1%)	115 (2%)
Non-Hispanic black	1093 (3%)	299 (4%)	246 (4%)
Non-Hispanic white	30 677 (90%)	5984 (88%)	6091 (90%)
Pacific Island	177 (1%)	43 (1%)	39 (1%)
Some college-level education	24 128 (71%)	4373 (64%)	5171 (76%)
Body-mass index (kg/m^2)	27·2 (4·7)	27·4 (4·8)	27·0 (4·8)
Vigorous physical activity ⩾1h/week	29 267 (86%)	4535 (67%)	6057 (89%)
Aspirin use >1 times/week	13 075 (38%)	2676 (39%)	3190 (47%)
Ibuprofen use >1 times/week	6086 (18%)	1352 (20%)	1334 (20%)
Smoking status			
Ever	18 172 (54%)	4037 (59%)	3433 (49%)
Current	2785 (7%)	842 (12%)	303 (4%)
Alcohol ⩾15 g/day	7186 (21%)	1461 (22%)	1355 (20%)
Total caloric intake (kcal/day)	2052 (792)	1378 (555)	2826 (557)
Red meat (g/day)	76·7 (64·4)	102·6 (54·1)	44·0 (56·2)
Folate (μg/day)	621 (362)	464 (376)	844 (390)
Calcium (mg/day)	1274 (619)	1148 (581)	1401 (603)

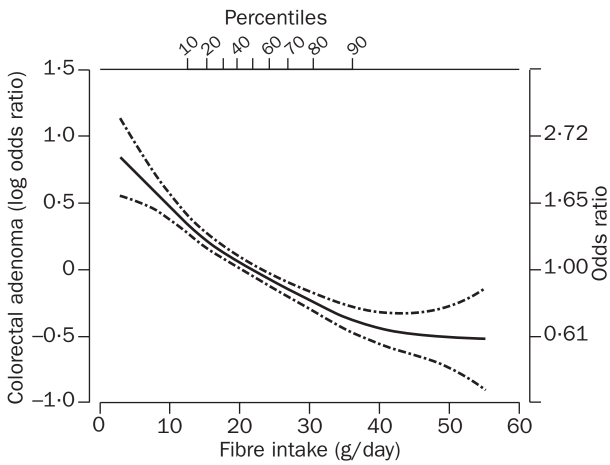
All values other than age and sex were standardised for age and sex. Red meat, folate, and calcium intake were also standardised for energy intake. Values are mean (SD) or number of participants (%).

Table 1: **Distribution of study characteristics**

For personal use. Only reproduce with permission from The Lancet Publishing Group.

Full multivariate logistic models were calculated, with additional adjustment for ethnic origin (American Indian or Alaskan native, Asian, Hispanic, non-Hispanic black, non-Hispanic white, or Pacific Islander), educational attainment (<8 years school, 8–11 years school, 12 years school or high-school equivalent, post-high school other than college, some college, college graduate, postgraduate), smoking (never, smoked cigar or pipe, quit smoking ⩾20 years ago and ⩽1 pack/day, quit ⩾20 years ago and >1 pack/day, quit <20 years ago and ⩽1 pack/day, quit <20 years ago and >1 pack/day, or unknown), alcohol use (<1 g/day, ⩾1–15 g/day, >15–30 g/day, >30 g/day), use of aspirin and ibuprofen separately (no regular use, <2 times per month, 2–3, 4, 8, 12–16, 30, 60 per month), physical activity (no, <1 h, 1 h, 2 h, 3 h, ⩾4 h of vigorous activity per week), body-mass index (kg/m^2), red meat intake (g/day), calcium intake (mg/day), and folate intake (μg/day). We chose the factors included in the full multivariate models on the basis of a-priori hypotheses for colorectal adenoma and cancer risk factors. Linear dose-response relations were tested, treating fibre as a continuous variable in logistic regression models. Stratified analyses were used to explore the modifying effects on the fibre-adenoma association from sex, age, smoking status, body-mass index, aspirin and ibuprofen use, red meat, fat, folate, and calcium. To test whether the odds ratios for adenoma subgroups (advanced *vs* non-advanced, colon *vs* rectum) differed significantly, we did logistic regression analyses comparing different case-groups with each other.

If less than 1% of the data for a variable was missing, missing values were imputed from the mean (for continuous variables) or mode (for categorical variables) of known values; otherwise, we included an extra category for missing values. Models including and excluding participants with missing information were similar with respect to the association between fibre and adenoma. All p values were two-tailed.



Total dietary fibre (g/day) and distal colorectal adenoma (kernel smoothing)

Median fibre intake odds ratio=1·0 (reference), fibre intake, adjusted for energy intake. Dotted lines are 95% CI. The 1% of participants with the highest fibre intake (>55·3 g per day) were not plotted to reduce the graphical weight of the extreme upper values.

Role of the funding source

All parts of the study described in the report on fibre and colorectal adenoma, including design, running of the trial, data management, data analysis, and preparation of the report, were funded by the US National Cancer Institute.

Results

The range of total dietary fibre intake in the study population for the 10th to 90th percentiles was 12·6–36·4 g/day (median 21·9; based on controls). Study participants in the highest quintile of dietary fibre intake were slightly older, less likely to be female, and more educated than those in the lowest quintile (table 1). People who had high-fibre diets also exercised more, smoked less,

	Quintiles of fibre intake (number of controls)					
	1 (n=6793)	2 (n=6795)	3 (n=6795)	4 (n=6794)	5 (n=6794)	p_{trend}
All colorectal adenoma						
Cases	825	739	709	681	637	
Base model odds ratio (95% CI)*	1·00	0·79 (0·71–0·89)	0·70 (0·62–0·78)	0·59 (0·53–0·67)	0·47 (0·40–0·54)	<0·0001
Multivariate-adjusted odds ratio (95% CI)†	1·00	0·91 (0·81–1·01)	0·85 (0·76–0·96)	0·79 (0·69–0·90)	0·73 (0·62–0·86)	0·002
Colon adenoma‡						
Cases	554	498	468	446	412	
Base model odds ratio (95% CI)*	1·00	0·80 (0·70–0·91)	0·69 (0·60–0·79)	0·59 (0·50–0·68)	0·45 (0·38–0·54)	<0·0001
Multivariate-adjusted odds ratio (95% CI)†	1·00	0·91 (0·80–1·04)	0·84 (0·73–0·97)	0·77 (0·66–0·90)	0·70 (0·58–0·85)	0·0006
Rectal adenoma						
Cases	144	132	133	127	123	
Base model odds ratio (95% CI)*	1·00	0·83 (0·65–1·06)	0·78 (0·61–1·01)	0·69 (0·52–0·90)	0·59 (0·43–0·81)	0·002
Multivariate-adjusted odds ratio (95% CI)†	1·00	0·94 (0·74–1·21)	0·96 (0·74–1·26)	0·91 (0·68–1·22)	0·93 (0·65–1·33)	0·97
Non-advanced adenoma§						
Cases	476	446	435	445	392	
Base model odds ratio (95% CI)*	1·00	0·82 (0·72–0·94)	0·73 (0·63–0·84)	0·66 (0·57–0·77)	0·48 (0·40–0·58)	<0·0001
Multivariate-adjusted odds ratio (95% CI)†	1·00	0·94 (0·82–1·08)	0·89 (0·77–1·03)	0·87 (0·74–1·02)	0·74 (0·61–0·91)	0·02
Advanced adenoma¶						
Cases	348	293	275	236	245	
Base model odds ratio (95% CI)*	1·00	0·75 (0·64–0·89)	0·65 (0·54–0·77)	0·50 (0·41–0·60)	0·44 (0·35–0·55)	<0·0001
Multivariate-adjusted odds ratio (95% CI)†	1·00	0·86 (0·73–1·02)	0·81 (0·67–0·97)	0·67 (0·55–0·83)	0·71 (0·55–0·91)	0·03

Cut points of quintiles of fibre intake were 15·4 g per day, 19·8 g per day, 24·3 g per day, 30·6 g per day. *Adjusted for age, sex, centre, and energy intake. †Adjusted for age, centre, sex, and energy intake. ‡Colon adenoma=adenoma of the sigmoid or descending colon; cases with adenomas in both rectum and colon were excluded. §Non-advanced adenoma=small (<1 cm), no high-grade dysplasia, and no villous elements. ¶Advanced adenoma=large (⩾1 cm), high-grade dysplasia, or villous elements (including tubulovillous adenomas).

Table 2: **Association between total dietary fibre and distal colorectal adenoma**

For personal use. Only reproduce with permission from The Lancet Publishing Group.

	10% and 90% percentiles (g/day)	Base model*		Multivariate-adjusted analyses†	
		Odds ratio (95% CI)	p_{trend}	Odds ratio (95% CI)	p_{trend}
Fibre source					
Total fibre	12·6–36·4	0·77 (0·73–0·81)	<0·0001	0·91 (0·86–0·97)	0·002
Fibre from:					
Grains/cereals	3·3–14·1	0·75 (0·68–0·82)	<0·0001	0·88 (0·79–0·97)	0·008
Legumes	0·9–5·6	0·88 (0·73–1·67)	0·22	0·99 (0·78–1·20)	0·90
Vegetables	2·7–10·7	0·96 (0·84–1·10)	0·59	1·00 (0·89–1·15)	0·99
Fruits	1·4–8·7	0·58 0·51–0·67)	<0·0001	0·80 (0·71–0·93)	0·003

*Adjusted for age, centre, sex, and energy intake. †Adjusted for age, centre, sex, energy intake, ethnic origin, education attainment, smoking, alcohol intake, aspirin use, ibuprofen use, physical activity, body-mass index, red meat intake, folate intake, calcium intake, and other fibre food sources (for analysis of fibre from grains and cereals, legumes, vegetables and fruits).

Table 3: **Association between fibre food groups and distal colorectal adenomas**

drank less alcohol, used aspirin more frequently, and reported a higher dietary intake of folate and calcium and lower intake of red meat (table 1).

Risk for colorectal adenoma decreased with increasing fibre intake, based on non-parametric (figure) and multivariate-adjusted parametric analyses (p=0·002), with steadily decreasing adenoma risks for each quintile of increasing fibre intake (table 2). In multivariate analysis, participants in the highest quintile of fibre intake had a 27% decrease in adenoma risk compared with those in the lowest quintile, related to an increase in fibre intake of about 24 g/day. These reductions were similar for men (26%, 95% CI 10–40) and women (26%, 1–45).

The inverse associations for dietary fibre were much the same for risk of advanced and non-advanced adenoma (table 2). The protective association of fibre was present for adenoma of the colon; adenoma of the rectum was not associated with fibre intake after multivariate adjustment (p=0·97). The difference in dose-response for rectal adenoma versus colon adenoma was not significant in multivariate analysis (p=0·06).

Total fibre and fibre from grains/cereals and fruits, but not from legumes or vegetables, were associated with adenoma risk (table 3). Adding each of the 11 a-priori potential confounders that were included in the multivariate-adjusted model one at a time to the base model (adjusted for age, sex, centre, and energy), indicated that smoking was the strongest single confounder. Adenoma risk in the highest, compared with the lowest, quintile of fibre intake was 0·47 (95% CI 0·40–0·54) for the base model and 0·57 (0·50–0·67) for the base model plus additional adjustment for smoking. The next strongest risk factor was folate, followed by red meat, physical activity, and alcohol intake, which resulted in odds ratios between 0·50 and 0·51. These five factors accounted for almost all of the attenuation in the fibre-adenoma association seen in the multivariate model compared with the base model. In stratified analyses, we found no evidence that the association between total dietary fibre and adenoma was modified by sex, age, smoking status, body-mass index, aspirin and ibuprofen use, intake of red meat, fat, folate, or calcium (data not shown).

Discussion

In this large study with over 3500 adenoma cases, risk of distal adenoma decreased with increasing intake of dietary fibre in both men and women. Advantages of our study are the large number of participants, the large number of distal adenoma cases, a wide range of fibre intake, and the standardised screening procedure for endpoint ascertainment.

The study, with inclusion of participants from diverse regions of the USA, meant that we could investigate the association between fibre and adenoma over a range of fibre intakes that encompasses average fibre consumption for the US population (16 g/day),[25] and the high fibre intake (about 30–35 g/day) recommended in current guidelines[26] and achieved by the intervention groups in clinical trials.[16,17] Few participants, however, reported fibre intake at the level reported for African populations with a vegetable-rich diet (eg, >50 g fibre/day),[27] among whom the fibre hypothesis was first developed.[1]

Earlier studies have been criticised for limited adjustment of potentially confounding risk factors.[14] In our population, adjusting for several known and potential dietary and non-dietary risk factors attenuated the association between fibre and adenoma; however, a protective association between fibre and adenoma risk remained. Models incorporating many covariates might give biased estimates of relative risk because of accumulated errors introduced by each of these covariates and their intercorrelations,[28] possibly accounting for some of the attenuation we observed in risk in the multivariate-adjusted, compared with the base, models.

In our study, fibre intake was not clearly associated with reduced risk for rectal adenoma. The Health Professionals Follow-up Study (HPFS)[13] also reported an association of fibre with adenoma of the distal colon, but not of the rectum. The absence of an association between fibre and rectal adenoma could reflect local differences in bowel milieu, including faecal water content, transit time of faeces, and gut flora. In our study, the association between fibre and adenoma risk did not significantly differ for advanced and non-advanced adenoma. Similar results were reported in three case-control studies.[3,12,29] Although differential risks by morphological characteristics could have been attenuated because of misclassification of tumour characteristics,[30] the results suggest that fibre affects tumour progression from its early stages.

Results of several case-control studies[3–12] have generally supported the hypothesis that greater fibre intake reduces risk for colorectal adenoma. Some of these studies,[4,7–9,12] however, showed no linear trend and imprecise estimates. In the Nurses Health Study,[14] dietary fibre was not associated with adenoma risk, whereas in the HPFS,[13] total fibre and fruit fibre were weakly inversely associated with frequency of adenoma. The Nurses Health Study and the HPFS were not done in a screening programme and the adenoma analysis included cohort members who underwent colon examinations for various reasons. The HPFS reported that the inverse associations of total fibre and fruit fibre with adenoma risk were strongest in men who had a negative endoscopy at some point before study entry, raising the possibility of a stronger effect of fibre for recently developed lesions compared with lesions that had developed some time ago.[13] Our investigation, assessing risk in participants with a negative examination up to 3 years before the study, found no additional protective effects in this group (data not shown).

We have shown a protective association of dietary fibre from fruits and grains with adenoma risk, independent of several dietary factors, including folate, a nutrient present in fruits and vegetables and which is of particular interest for colon carcinogenesis.[31] Nevertheless, fibre might also be a

For personal use. Only reproduce with permission from The Lancet Publishing Group.

marker for unmeasured substances that have anticarcinogenic effects and occur jointly with fibre, in particular fibre from fruits and grains.

Results of two randomised clinical trials[16,17] showed no effect of increased fibre intake on colorectal adenoma recurrence. Although non-randomised observational studies, like ours, cannot rule out confounding with the same degree of certainty as randomised trials, our study has the advantage that some study members may have consumed high-fibre diets for many years. Thus, the duration of high-fibre intake could be substantially greater in our study than the 3–4 years study periods of the polyp trials.[16,17]

We focused on differences in fibre intake between participants with distal adenomas compared with controls who screened negative by sigmoidoscopy for polyps in the distal colon. We expect that some controls had unrecognised right-sided adenomas. Assuming that fibre has a similar effect on right-sided polyps (as suggested by our analyses on cases with right-sided adenoma only, data not shown), the existence of these false-negative controls would have only attenuated the true inverse association between fibre and adenoma risk.

In a screening trial of this nature, not all participants can be clearly categorised as cases or controls. As an exploration of the robustness of our findings, sequentially including participants with hyperplastic polyps, tumours of unknown histology or location, or positive screening with no endoscopy follow-up into the case or control group did not change the risk estimate appreciably (data not shown). Also some participants were aware of the initial sigmoidoscopy screening examination result at the time of the dietary assessment, however, no large differences were noted in the fibre-adenoma association in those who completed the dietary examination before (n=10 588, 28%), on the day of (n=21 264, 57%), or after the day of (n=5710, 15%) the sigmoidoscopy screening examination.

Adenomas identified on an initial screening might have developed some years previously. Whether fibre affects adenoma formation or subsequent persistence of the lesion (duration) is difficult to assess, however, finding an inverse association for small (non-advanced) adenoma suggests that high-fibre diet is protective from the earlier stages of adenoma formation. In our study, high intakes of dietary fibre, especially from grains, cereals, and fruits, was associated with lower risk of colon adenoma.

Contributors

All authors had the idea for the study and contributed to study design, data analysis, and writing of the report.

Conflict of interest statement

None declared.

Acknowledgments

The Prostate Lung Colorectal and Ovarian Cancer Screening Trial is fully funded by the National Cancer Institute, National Institutes of Health, Department of Health and Human Services of the US government.

References

1 Burkitt DP. Epidemiology of cancer of the colon and rectum. *Cancer* 1971; **28:** 3–13.
2 Kim YI. AGA technical review: impact of dietary fiber on colon cancer occurrence. *Gastroenterology* 2000; **118:** 1235–57.
3 Breuer-Katschinski B, Nemes K, Marr A, et al, for the Colorectal Adenoma Study Group. Colorectal adenomas and diet: a case-control study. *Dig Dis Sci* 2001; **46:** 86–95.
4 Lubin F, Rozen P, Arieli B, et al. Nutritional and lifestyle habits and water-fiber interaction in colorectal adenoma etiology. *Cancer Epidemiol Biomarkers Prev* 1997; **6:** 79–85.
5 Haile RW, Witte JS, Longnecker MP, et al. A sigmoidoscopy-based case-control study of polyps: macronutrients, fiber and meat consumption. *Int J Cancer* 1997; **73:** 497–502.
6 Martinez ME, McPherson RS, Annegers JF, Levin B. Association of diet and colorectal adenomatous polyps: dietary fiber, calcium, and total fat. *Epidemiology* 1996; **7:** 264–68.
7 Neugut AI, Garbowski GC, Lee WC, et al. Dietary risk factors for the incidence and recurrence of colorectal adenomatous polyps: a case-control study. *Ann Intern Med* 1993; **118:** 91–95.
8 Sandler RS, Lyles CM, Peipins LA, McAuliffe CA, Woosley JT, Kupper LL. Diet and risk of colorectal adenomas: macronutrients, cholesterol, and fiber. *J Natl Cancer Inst* 1993; **85:** 884–91.
9 Little J, Logan RF, Hawtin PG, Hardcastle JD, Turner ID. Colorectal adenomas and diet: a case-control study of subjects participating in the Nottingham faecal occult blood screening programme. *Br J Cancer* 1993; **67:** 177–84.
10 Kune GA, Kune S, Read A, MacGowan K, Penfold C, Watson LF. Colorectal polyps, diet, alcohol, and family history of colorectal cancer: a case-control study. *Nutr Cancer* 1991; **16:** 25–30.
11 Macquart-Moulin G, Riboli E, Cornee J, Kaaks R, Berthezene P. Colorectal polyps and diet: a case-control study in Marseilles. *Int J Cancer* 1987; **40:** 179–88.
12 Hoff G, Moen IE, Trygg K, et al. Epidemiology of polyps in the rectum and sigmoid colon. Evaluation of nutritional factors. *Scand J Gastroenterol* 1986; **21:** 199–204.
13 Platz EA, Giovannucci E, Rimm EB, et al. Dietary fiber and distal colorectal adenoma in men. *Cancer Epidemiol Biomarkers Prev* 1997; **6:** 661–70.
14 Fuchs CS, Giovannucci EL, Colditz GA, et al. Dietary fiber and the risk of colorectal cancer and adenoma in women. *N Engl J Med* 1999; **340:** 169–76.
15 McKeown-Eyssen GE, Bright-See E, Bruce WR, et al, for the Toronto Polyp Prevention Group. A randomized trial of a low fat high fibre diet in the recurrence of colorectal polyps. *J Clin Epidemiol* 1994; **47:** 525–36.
16 Schatzkin A, Lanza E, Corle D, et al, for the Polyp Prevention Trial Study Group. Lack of effect of a low-fat, high-fiber diet on the recurrence of colorectal adenomas. *N Engl J Med* 2000; **342:** 1149–55.
17 Alberts DS, Martinez ME, Roe DJ, et al, for the Phoenix Colon Cancer Prevention Physicians' Network. Lack of effect of a high-fiber cereal supplement on the recurrence of colorectal adenomas. *N Engl J Med* 2000; **342:** 1156–62.
18 MacLennan R, Macrae F, Bain C, et al, for the Australian Polyp Prevention Project. Randomized trial of intake of fat, fiber, and beta carotene to prevent colorectal adenomas. *J Natl Cancer Inst* 1995; **87:** 1760–66.
19 Bonithon-Kopp C, Kronborg O, Giacosa A, Rath U, Faivre J, for the European Cancer Prevention Organisation Study Group. Calcium and fibre supplementation in prevention of colorectal adenoma recurrence: a randomised intervention trial. *Lancet* 2000; **356:** 1300–06.
20 Bingham SA, Day NE, Luben R, et al. Dietary fibre in food and protection against colorectal cancer in the European Prospective Investigation into Cancer and Nutrition (EPIC): an observational study. *Lancet* 2003; **361:** 1496–501.
21 Gohagan JK, Prorok PC, Hayes RB, Kramer BS. The Prostate, Lung, Colorectal and Ovarian (PLCO) Cancer Screening Trial of the National Cancer Institute: history, organization, and status. *Control Clin Trials* 2000; **21:** S251–72.
22 Hayes RB, Reding D, Kopp W, et al. Etiologic and early marker studies in the prostate, lung, colorectal and ovarian (PLCO) cancer screening trial. *Control Clin Trials* 2000; **21:** S349–55.
23 Subar AF, Midthune D, Kulldorff M, et al. Evaluation of alternative approaches to assign nutrient values to food groups in food frequency questionnaires. *Am J Epidemiol* 2000; **152:** 279–86.
24 Tippett KS, Cypel YS. Design and operation: the continuing survey of food intakes by individuals and the diet and health knowledge survey, 1994–96. In: Continuing survey of food intakes by individuals 1994–96. Nationwide Food Surveys Rep No 96-1. US Department of Agriculture, Agricultural Research Service, 1998.
25 US Department of Agriculture, Agricultural Research Service. Data tables: food and nutrient intakes by individuals in the United States, by region, 1994–96. ARS Surveys Research Group, available on 'Topics of interest, table sets in PDF format' page at http://www.barc.usda.gov/bhnrc/foodsurvey/ (accessed March 23, 2003).
26 American College of Gastroenterology, American Gastroenterological Association medical position statement: impact of dietary fiber on colon cancer occurrence. *Gastroenterology* 2000; **118:** 1233–34.
27 Wolever TM, Jenkins DJ. What is a high fiber diet? *Adv Exp Med Biol* 1997; **427:** 35–42.
28 Wacholder S. When measurement errors correlate with truth: Surprising effects of nondifferential misclassification. *Epidemiology* 1995; **6:** 157–61.
29 Terry MB, Neugut AI, Bostick RM, et al. Risk factors for advanced colorectal adenomas: a pooled analysis. *Cancer Epidemiol Biomarkers Prev* 2002; **11:** 622–29.
30 Terry MB, Neugut AI, Bostick RM, Potter JD, Haile RW, Fenoglio-Preiser CM. Reliability in the classification of advanced colorectal adenomas. *Cancer Epidemiol Biomarkers Prev* 2002; **11:** 660–63.
31 Giovannucci E. Epidemiologic studies of folate and colorectal neoplasia: a review. *J Nutr* 2002; **132:** S2350–55.

For personal use. Only reproduce with permission from The Lancet Publishing Group.